REMARKS

Applicant thanks Examiner Pak for his thorough analysis of the application. In response to the Office Action mailed October 2, 2002, the application has been carefully reviewed and amended.

The Applicant understands that the Examiner has not examined claims 79 and 83 - 110 because he believes they are directed to an invention that is independent or distinct from the other examined claims and because his search does not cover the claimed invention. The Examiner has withdrawn Claims 79 and 83 - 110 from consideration as being dependent on a non-elected invention. 37 C.F.R. § 1.142(b). The Applicant has amended these claims to depend on Claim 79 (old Claim 80) so that they no longer depend from the withdrawn subject matter. Thus, only Claim 78 (old Claim 79) is in need of withdrawal pursuant to the Examiner's request.

Entry of the foregoing amendments and reconsideration of the application is respectfully requested.

Allowable Subject Matter

The Applicant has made the Examiner's recommended editorial changes discussed on pp. 2 - 6, including rewording the Markush language and renumbering the claims following Claim 50. The Applicant has amended Claim 14 to properly depend from Claim 12, not Claim 9.

Claims 42-78

The combination of NAD^+ and vanadyl sulfate, with proper language correction has been deemed allowable (Office Action dated July 8, 2003 [p. 3] and Office Action dated October 2, 2003).

The Examiner has stated that the new Claims 42 - 50 and 52 - 78 have been submitted on the allowable material but that editorial corrections are still needed. These corrections have been made, including adopting the corrected Markush language in Claims 43, 52, 58, 59, and 78, as well as in Claim 44. The Applicant has added the word "further" in Claims 47, 50, 61, 72, and made other

small editorial changes to better describe the invention and per the Examiner's request. The claims have been renumbered starting with 52 being renumbered as 51 and all dependent claims have been changed correspondently. The Applicant believes that all the claims having the combination of NAD^+ and vanadyl sulfate, with proper language corrections are now allowable, including Claims 42 - 50 and 52 - 78, which Applicant respectfully submits are in condition for allowance.

The Applicant notes that the Examiner has withdrawn the election of species requirement as to the metal ion/complex on the bottom of p. 2. This was handwritten by the Examiner and is made note of by the Applicant as not requiring us to elect a particular metal ion/complex species and to thus allowing all the claims with different metal ion/complexes to be examined.

Rejections Under 35 USC §112

The Claims that stood rejected under 35 USC §112, second paragraph or for other editorial concerns by the Examiner have been amended to recite a proper and definite Markush group. Thus, the rejection of these claims under 35 U.S.C. § 112 is believed to have been overcome.

Claim 1 has been amended as discussed below. Claim 11 has had the word, "of alcohol" added to make clear what is being oxidized. The Examiner pointed out, there are many substances being oxidized and reduced, but as the Applicant believes it is clear from the specification that Claim 11 refers to the "oxidation of alcohol" but has amended Claim 11 to further clarify. Claims 79 - 81 (old Claims 80 - 82) have been rewritten in independent format since Claim 78 (old Claim 79) has been withdrawn by the Examiner. Claim 69 (old Claim 70) has been amended to define "derivatives and analogous thereof" and Claim 73 (old Claim 74) has been amended to supply the antecedent basis for "dehydrogenase."

Rejections Under 35 USC §102

Claims 1-3

Claims 1-3 still stand rejected under 35 USC §102(b) as being anticipated by or, in the alternative, under 35 USC §103(a) as obvious over Vadgama, et al. (WO 98/20332). The examiner relies upon Vadgama to disclose a solution mixture that contains potassium ferricyanide and NAD^+, citing examples two and three on pages 9-10 of Vadgama.

As the Applicant discussed in a prior response, Vadgama is directed to a bio sensor having an enzyme layer and an outer diffusion limiting barrier membrane wherein detectors are located on opposing sides of the enzyme layer and the diffusion limiting barrier membrane. The enzyme layer incorporates an enzyme capable of interacting with a selected analyte.

Vadgama impregnates the enzyme laminate with lactate dehydrogenase and NAD+. Alternatively, the enzyme laminate is fabricated with malate dehydrogenase and NAD+. (Page 9-10)

While the Examiner is correct on page 6 in stating that Vadgama et al. discusses a solution mixture of potassium ferricynide and NAD^+, the purpose of that solution (in the presence of a substrate) is to measure the activity of a analyte (or in the presence of a dehydrogenase). There is no reason to imply that a composition is formed or that there is oxidation of the substrate (in this case, alcohol). In fact, the disclosure teaches away from the formation of our composition since the purpose of Vadgama is to allow the analyte through the membrane.

Vadgama makes clear on page 2 - 3, that the biosensor comprises an enzyme layer capable of interacting with an analyte to provide a detectable change. Detecting means on one side of a layer for detecting said change, and an outer diffusion limiting barrier membrane on the opposite side of said layer incorporating this effect to render it permeable to the analyte. Table 1 on page 3 makes clear that the enzyme such as lactate dehydrogenase or malate

dehydrogenase has to be capable for interacting with the analyte such as lactate of malate respectively. Not only must the enzyme be present, but the enzyme co-factor such as diaphorase, potassium ferricynide and NAD^+ must also be present in order for the sensor to work. The enzyme interacts with the analyte, lactate, or malate and not with the NAD^+ according to the invention of Vadgama.

Our invention, as shown in amended Claim 1, recites in part that, "NAD^+ a catalyst from at least one of the species of a multivalent transition metal ion, or a complex thereof, is selected to accelerate the in vivo oxidation of an alcohol in the absence of a dehydrogenase." This is clearly in contrast to what Vadgama states in his patent. There is no indication that the composition without a dehydrogenase such as formed with a lactate or mulate presence would be effective. Thus, it cannot be the same composition. Also, Vadgama does not even disclose acceleration of oxidation of alcohol in the absence of a dehydrogenase and it has to teach away from such teaching because Vadgama states that the dehydrogenase must be present to interact with the enzyme cofactor listed in Table 1 or similar cofactors. Applicant respectfully submits that Claim 1 is distinguishable from that of Vadgama and since Claims 2 and 3 depend from Claim 1, include all the limitations thereof. Applicant respectfully submits that these claims as also in condition for allowance.

These chemicals are selected to provide an electrochemical means preferably of the non potentiometric, wherein amperometric detection is preferred. (Vadgama, Page 6)

Claims 1-2, 4-11, 15, 17-19, 22-23, and 34-35

Claims 1-2, 4-11, 15, 17-19, 22-23, and 34-35 still stand rejected under 35 U.S.C. §102(b) as anticipated by, or in the alternative, under 35 U.S.C. §103 as obvious over Blass (U.S. Patent No. 5,053,396) for "reasons of record." (Office Action dated July 8, 2003, Page 7, Paper 2, Page 6).

Examiner Pak relies upon Col. 5, Lines 37-61 to disclose the recited constituents.

The components as indicated are mixed together and formulated to the desired therapeutic compositions in a manner well known in the art.

Preferred and minimum dosages for the components to be included within the composition (per dose) are indicated below without limiting the invention.

Component	Preferred dosage	Range
Acetylsalicylic acid	600–900 mg	300–1000 mg
or Ibuprofen	150–200 mg	100–300 mg
or Fenoprofen calcium	300–600 mg	200–800 mg
Nicotinamide	300–500 mg	70–1500 mg
NAD	100–200 mg	70–300 mg
Pantothenic acid	100–400 mg	50–500 mg
Riboflavin	30–60 mg	5–100 mg
Pyridoxine HCl	30–60 mg	5–100 mg
Thiamine HCl	70–150 mg	50–600 mg
Ascorbic acid	250–500 mg	100–800 mg
Fructose	5000 mg	2000–15000 mg
Promethazine HCl	25 mg	10–50 mg
or Chlorpheniramine maleate	4 mg	2–6 mg
Sodium bicarbonate	—	0–4000 mg
Potassium bicarbonate	—	0–4000 mg
Magnesium carbonate	—	0–4000 mg
or Magnesium oxide or hydroxyde	—	0–4000 mg
Calcium carbonate	—	0–4000 mg
Citric acid	1200–1800 mg	0–4000 mg
Zinc ions	1,5 mg	0,5–20 mg
Iron ions	10 mg	5–30 mg
Mangenese ions	0,6 mg	0,3–1,0 mg
Chromium ions	1 mcg	1 mcg
Sweetening or flavouring agents and other additives	as required	

Any of the metals mentioned in this specification could be present wholly or partly as the salts of gluconic, levulinic, ascorbic, citric or phosphoric acids, or any other suitable acids, where this would be advantageous. They could also be present wholly or partly as amino acid chelates.

The Examiner stated that "Applicant asserts that iron ions and chromium ions in Blass's composition would be reduced by a ascorbic acid and thus would not exist in the ion or complex ion state. A review of page 13 of the October 2002 Office Action Response finds that the Applicant submits that "Blass does not disclose the recited multivalent transition metal ions, or complexes thereof." On page 14 of the October 2002 Office Action Response a review of the specification verifies that the "zinc and manganese ions in Blass are a one valent state metal and thus are not a multivalent transition metal ion." Therefore, the recited zinc and manganese ions in Blass cannot act as a catalyst in the redox reaction.

The Applicant wants the Examiner to know that the addition of ascorbic acid in Blass would "reduce both these metals to a reduced state." The Applicant did not mean to imply that the "iron ions and chromium ions in the Blass composition would be reduced by ascorbic acid." Rather, the Applicant believes that the irons would be reduced from the ferric (III) oxidation state to the ferrous (II) state which would not act as an accelerator or indeed be able to function as a pseudo-dehydrogenase.

The Examiner suggests that the ascorbic acid would be "neutralizing" by the sodium carbonate or calcium carbonate discussed in the Blass patent. Such neutralization would result in ascorbate ion which is a much more powerful reducing agent than ascorbic acid itself. As predicted from the Nernst equation which predicts that reducing agents become more efficient in alkaline Ph. The Examiner maintains that the presence of manganese (assuming it is Manganic (III) oxidation state, though not stated by Blass) would "neutralize the ascorbic acid. The relative amount of ascorbic acid that would be sufficient to reduce both NAD^+ and Manganic (III) ions to the Manganous (II) state. As indicated from a search on MedLine, indicated that there is no known reference to the interaction of manganous ions with reductions by ascorbic acid; there are also no such references by inference to zinc. Thus, it is difficult for the Applicant to understand why the Examiner believes that "the other components in Blass's composition, such as sodium carbonate, calcium carbonate, zinc, and manganese, could neutralize ascorbic acid" since Applicant is not aware of a reference that seems to indicate that such would occur.

The Examiner also claims that the "Applicant's argument is not consistent with Applicant's own claims." The Examiner uses Claim 21 as an example since it permits the presence of "other antitoxins such as isoflavanoids." The Applicant wants to explain that while some antitoxins may act as mild reducing agents, not all antitoxins can be classified as reducing agents. The relative amounts the Agent would preclude the possibility of reducing all of the NAD^+ or the ferric ions. Once again, a search on MedLine shows no reference to the reduction of NAD^+ or ferric ions by the example chosen by the Examiner, i.e., isoflavanoids, nor

other references to any such reduction by any of the other additives cited in our subsequent claims. The Applicant cannot find any reference to the reduction of any of the additives cited in our subsequent claims in prior art.

The Examiner's interpretation of Blass to disclose the composition of our invention is certainly confusing to the Applicant. Patent law states that an invention is patentable unless it is shown to be unpatentable by the Examiner. The Applicant is not familiar with the statutory law that allows a patent to be rejected because "the composition is not certain enough to exclude Blass, composition from consideration herein." There are not quantitative or semi-quantitative evidence that such effects were predicted or even seen in the Blass invention. There certainly was no attempt to measure the blood alcohol level (not even crudely using a breathalyzer) after the application of the Blass formula.

The Applicant's invention is based on facts that resulted from more than three years in the development of a thin film essay for alcohol. Therefore, applicant respectfully submits as amended, Claim 1 distinguishes over Blass.

As Claims 2, 4-11, 15, 17-19, 22-23 and 34-35 depend from Claim 1 and include all limitations thereof, applicant respectfully submits these claims are also in condition for allowance.

Claims 1 and 2

Claims 1 and 2 are also rejected under 35 U.S.C. § 102(b) as being anticipated by Crans et al. because Crans explicitly discloses, according to the Examiner, analytical grade solution of a vanadate and NAD, i.e. NAD^+. The Examiner actually admits "the disclosed composition does not expressly disclosed is a composition for accelerating in-vivo oxidation of the alcohol." The Examiner seems to think that this is the same composition. The Examiner is failing to distinguish between the oxidation states that are so important to understanding the chemistry of our invention. Vanadate is a (V) (even - electron) oxidation state while vanadyl sulfate is the (IV) (odd - electron) oxidation state. Contrary to the Examiner's understanding, the composition in Crans could not act as a composition and the Applicant's invention does. An organic chemistry test

would show that sodium vanadate is a powerful oxidation agent, and thus, vanadate perchlorate, persulfate , permanganate, chromate or chlorate oxidize ethol alcohol directly to acetic acid and thus cannot act as a catalyst or pseudo-enzymes. In fact, early, less reliable breathalyzers were based on the oxidation of ethanol by potassium chromate. Crans et al. must, therefore, be described to case specific to glucose-6-phosphate or something of this sort which is distinguishable from the current invention. Crans et al. poses a mechanism for the catalytic action of vanadate involving the formulation of vanadate esters. No such esters are known to exist for vanadaim (IV).

In fact, the Applicant brings to the Examiner's attention that in order to achieve a non-catalytic toxidation of 0.08% alcohol (corresponding to 650 mm) at least 10.5 grams of sodium vanadate. $NaVO^3$, would have to be used. This amount would not be safe for in vivo administration contrary to the Examiner's comments. To speculate that simply because "analytical solution for NMR study and thus is typically ultra-pure , and thus safe enough for in vivo" administration, is an erroneous statement by the Examiner. The equivalent amount of vanadyl sulfate would be 13 grams when the maximum recommended daily dose of 100M. This would not be safe for human consumption.

Withdrawn Claims

Claims 79-110

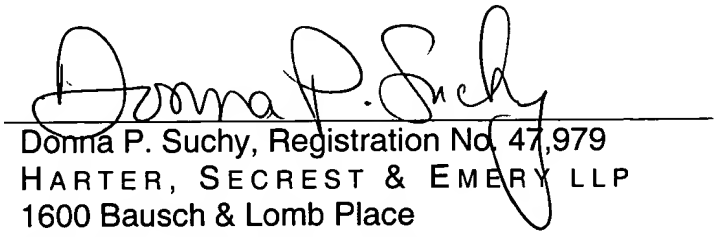
Since Claims 78 - 109 (old Claims 79-110) recite in part "a composition for accelerating in vivo oxidation of alcohol, the composition comprising NAD^+ in one of acetaldehyde dehydrogenase and alcohol dehydrogenase," the Examiner requested these claims be withdrawn.

As explained above, the amended claims no longer make reference to material that they Examiner stated had to be withdrawn.

Therefore, applicant respectfully submits all the pending claims, Claims 1-36 and 42-110 are in condition for allowance. If, however, the examiner feels

that any further issues remain, he is cordially invited to contact Donna Suchy so that such matters may be promptly resolved.

Respectfully submitted,



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